

US Patent Application No. 10/663,506  
Response to OA mail date 11/15/2006  
February 9, 2007

### **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### **Listing of Claims:**

1 (Currently Amended). A solid pharmaceutical composition for oral administration comprising a granulation, said granulation comprising rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid,

a water soluble polymer in an amount of about 1 % to about 40% (wt/wt),

a surfactant in an amount of about 1 % to about 8% (wt/wt), an antioxidant from 0.001% to 3% (wt/wt), and a pH modifying agent.

2 (Original). The composition of claim 1, wherein the water soluble polymer is PVP, hydroxypropylmethylcellulose, polyethylene glycol, or cyclodextrin or mixtures thereof.

3 (Original). The composition of claim 2, wherein the water soluble polymer is PVP.

4 (Currently Amended). The composition of claim 1 3, wherein the surfactant is polysorbate 80, sodium lauryl sulfate, sodium dodecyl sulfate, a salt of a bile acid, an ethoxylated vegetable oil, a polyoxyethylene-polyoxypropylene block copolymer, or a poloxamer.

5 (Original). The composition of claim 4, wherein the surfactant is sodium lauryl sulfate or sodium dodecyl sulfate.

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6 (Currently Amended). The pharmaceutical composition of claim 1 5, wherein the pH modifying agent is sodium citrate, citric acid, or dilute hydrochloric acid.

Claims 7 - 9. Cancelled.

10 (Previously Presented). A rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid oral composition prepared by the process comprising:

- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water;
- (c) combining the aqueous and alcoholic solutions to provide a hydrocoholic solution;
- (d) adding the hydroalcoholic solution to a mixer containing one or more intragranular excipients;
- (e) granulating the mixture; and
- (f) drying the resulting granulation.

11 (Original). The composition of claim 10, wherein the pH modifying agent is selected from the group consisting of citric acid, sodium citrate, hydrochloric acid and mixtures thereof.

12 (Original). The composition of claim 11, wherein the alcohol is ethanol.

13 (Original). The composition of claim 12, wherein the antioxidant is butylated hydroxyanisole and butylated hydroxytoluene.

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14 (Original). The composition of claim 13, wherein the surfactant is sodium lauryl sulfate.

15 (Previously Presented). A rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid oral formulation prepared by the process comprising:

- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water;
- (c) adding the aqueous and alcoholic solutions stepwise, and in one or more portions each, to a mixer containing one or more intragranular excipients;
- (d) granulating the mixture; and
- (e) drying the resulting granulation.

16 (Original). The composition of claim 15, wherein the pH modifying agent is selected from the group consisting of citric acid, sodium citrate, hydrochloric acid and mixtures thereof.

17 (Original). The composition of claim 16, wherein the alcohol is ethanol.

18 (Original). The composition of claim 17, wherein the antioxidant is butylated hydroxyanisole and butylated hydroxytoluene.

19 (Original). The composition of claim 18, wherein the surfactant is sodium lauryl sulfate.

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20 (New). The pharmaceutical composition according to claim 1, comprising  
rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-  
methylpropionic acid present in an amount of about 1% (wt/wt) to about 5% (wt/wt),  
polyvinylpyrrolidone in an amount of about 5% (wt/wt) to about 20%  
(wt/wt);  
a surfactant comprising sodium laurel sulfate in an amount of about  
3% to about 5% (wt/wt), and  
citric acid.